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FINAL REPORT

PUBLICATION/PATENTS/PRESENTATIONS/
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FOR

CONTRACT N00014-88-K-0315

R & T CODE 413P009-05

Biomimetic Catalysts for Hydrolysis (AASERT Award)

Cynthia J. Burrows

Research Foundation of SUNY

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December 31, 1995

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R&T Number: **413P009--05**

Contract/Grant Number: **B00014-88-K-0315**

Contract/Grant Title: **Biomimetic Catalysts for Hydrolysis**

Principal Investigator: **Cynthia J. Burrows**

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- a. Number of papers submitted to refereed journals, but not published: **0**
- b. Number of papers published in refereed journals: **3**
- c. Number of books or chapters submitted, but not yet published: **0**
- d. Number of books or chapters published: **0**
- e. Number of printed technical reports and non-refereed papers: **1**
 Tech. report no. 8: "Cyclization of Bis-Urethanes as a New Method for
 the Synthesis of 5-Substituted, 6-Membered Cyclic Ureas," 5/94.
- f. Number of patents filed: **0**
- g. Number of patents granted: **0**
- h. Number of invited presentations at workshops or professional society meetings: **1**
- i. Number presentations at workshops or professional society meetings: **4**
- j. Honors/Awards/Prizes for contract/grant employees: **None**
- k. Total number of Graduate Students and Post-Doctoral associates supported by at least
 25% during this period
 under this R&T project number:
 Graduate Students: **2**
 Post-Doctoral Associates: **0**
 including the number of
 Female Graduate Students: **2**
 Female Post-Doctoral Associates: **0**
 the number of
 Minority Graduate Students: **0**
 Minority Post-Doctoral Associates: **0**
 and the number of
 Asian Graduate Students: **0**
 Asian Post-Doctoral Associates: **0**
 [Note: one Hispanic undergraduate was also supported.]

- 1. Other funding: **see attached.**

Current Research Funding

1. National Institutes of Health, GM-47531, "Probing Guanine Structure in Nucleic Acid Folding," (with S. E. Rokita), \$771,238, 8/93 - 7/97.
2. National Science Foundation Career Advancement Award, CHE-9596059, "Using Cobalt to Probe DNA and RNA Folding," 7/93 - 12/95, \$37,000.
3. NATO Scientific Exchange Fellowship, "Steroidal Polyamines as Gene Transfer Vectors," (with J. P. Behr, Université Louis Pasteur, Strasbourg), 6/94 - 6/96, \$9,248.
4. National Science Foundation, CHE-9521216, "Biomimetic Oxidation Chemistry," 8/95-7/98, \$339,000.
5. National Institutes of Health, pending application, GM-49860, "Reactivity of Nickel Complexes with DNA," 4/96-3/99, \$532,194.
6. American Cancer Society, pending application, "Nickel Compounds in Carcinogenicity and Cancer Therapy," 7/96-6/98, \$200,000.

Part II

a. Principal Investigator: Cynthia J. Burrows

b. Current Telephone Numbers: 801-585-7290 (office), 801-581-8517 (secretary),
801-585-7868 (fax)

c. Cognizant ONR Scientific Officer: Harold E. Guard

d. Project Description:

Synthetic molecular receptors are of interest as tools for the selective detection of ions and molecules and as mimics of biological systems. One part of this project focuses on the use of cholic acid, a readily available steroid natural product, as the basic design element of new molecular receptors for the complexation of neutral organic molecules. Cholic acid is ideally suited to this task since, (i) it possesses a rigid hydrocarbon framework upon which hydrogen-bonding groups (hydroxyls) are appended in an orientation suitable for bonding to substrates, and (ii) considerably less synthetic effort is required to build a large receptor molecule than in the case of molecular receptors designed in an *ab initio* fashion. Molecular receptors are constructed from two cholic acid groups linked by a diamine group. The diamine linking groups under study include simple aromatic diamines providing a rigid spacer, diamines with additional ligating groups such as phenolate and carboxylate for ion-pairing with partially charged substrates, and diamines containing indicators or metal ions (p-nitrophenol, ferrocene, metal-salen complex). Substrates under study include simple diols and triols (ethylene glycol, glycerol), sugars (glucose, ribose), and amino-sugars (glucosamine). Results of these studies will lead to a better understanding of hydrogen bonding in non-polar solvents and to the development of chemical sensors for neutral polar molecules.

A second area of the project involves design and synthesis of dinucleating ligands capable of binding two transition metal ions for catalysis of hydrolytic reactions. The complexes utilize a difunctional mechanism to both coordinate and activate a carbonyl or phosphoryl oxygen in a Lewis acid sense, as well as binding and activating a water molecule. In this project, we use substituted ureas as the substrate of interest since they are notoriously difficult to hydrolyze. Also, it is known that the dinuclear metalloenzyme urease accelerates urea hydrolysis by a factor of 10^{14} using a dinuclear nickel center in the active site.

Burrows, Cynthia J.
December 31, 1995

e. Significant Results During the Project Period:

The major focus of our recent research has been in the synthesis of a new glucose receptor containing a transition metal binding site. The metal ion would serve to both organize the receptor for substrate binding as well as to eventually act as a Lewis acid for catalytic hydrolysis of bound glucosides. Progress in the synthesis of the compound has been achieved and binding studies are imminent.

In a second area, we have continued our study of dinuclear nickel and copper complexes capable of catalytic hydrolysis in which the substrate of choice is a urea. To this end, we have synthesized a series of cyclic ureas, some of which contain an intramolecular binding site for the metal ion. In the course of this study we discovered an unusual cyclization reaction of bis-urethanes that turns out to be a useful new synthetic method for cyclic ureas. This is reported in Technical Report no. 8.

f. Summary of Plans for the Next Year:

This is the end of the funded project.

g. Recent Graduate Students Working on the Project:

Ms. Kathy Fordon (5th year graduate student), Ph.D., December, 1994.

Mr. Greg Diaz (junior undergraduate)

Ms. Donna Iula (2nd year graduate student)

Recent Postdoctorals Working on the Project:

None

Publications citing support by this grant:

1. K. J. Fordon, C. G. Crane, and C. J. Burrows, "A Novel Method for the Synthesis of 5-Substituted 6-Membered Cyclic Ureas," *Tetrahedron Lett.* **1994**, 35, 6215-6216.
2. S. M. Evans, C. A. Venanzi, and C. J. Burrows, "Design of Cholic Acid Hosts for Molecular Recognition of Glucose using Systematic Conformational Searching," *J. Molec. Struct. (THEOCHEM)*, **1994**, 308, 159-174.
3. S. M. Evans, C. J. Burrows, and C. A. Venanzi, "Design of Cholic Acid Macrocycles as Hosts for Molecular Recognition of Monosaccharides," *J. Molec. Struct. (THEOCHEM)*, **1995**, 334, 193-205.